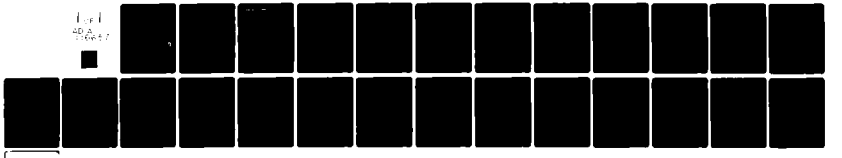
AD-A116 657 ARMY RESEARCH INST OF ENVIRONMENTAL MEDICINE NATICK MA F/G 6/19
RESPIRATORY ADAPTATION TO ACUTE METABOLIC ACIDOSIS IN GOATS WIT--ETC(U)
JUN 82 R A STEINBROOK, S HAVAHERI, R A GABEL

UNCLASSIFIED USARIEM-M-34/82 NL



END
DATE FILMED
7-82
DTIC

SECURITY CLASSIFICATION OF THIS PAGE *(When Data Entered)*

REPORT DOCUMENTATION PAGE

READ INSTRUCTIONS BEFORE COMPLETING FORM

1. REPORT NUMBER: M34/82	2. GOVT ACCESSION NO.: AD-A116657
3. RECIPIENT'S CATALOG NUMBER:	
4. TITLE *(and Subtitle)*: RESPIRATORY ADAPTATION TO ACUTE METABOLIC ACIDOSIS IN GOATS WITH ABLATED CAROTID BODIES	5. TYPE OF REPORT & PERIOD COVERED:
	6. PERFORMING ORG. REPORT NUMBER:
7. AUTHOR(s): R.A. Steinbrook, S. Havaheri*, R.A.Gabel, J.C. Donovan, D.E.Leith, and V. Fencl	8. CONTRACT OR GRANT NUMBER(s):
9. PERFORMING ORGANIZATION NAME AND ADDRESS: US Army Research Institute of Environmental Medicine, Natick, MA 01760	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: 3E1161102BS10 24182101002
11. CONTROLLING OFFICE NAME AND ADDRESS: U.S. Army Medical Research and Development Command Fort Detrick Frederick, MD 21791	12. REPORT DATE: 3 June 82
	13. NUMBER OF PAGES: 20
14. MONITORING AGENCY NAME & ADDRESS*(if different from Controlling Office)*:	15. SECURITY CLASS. *(of this report)*: Unclassified
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE:

16. DISTRIBUTION STATEMENT *(of this Report)*

Distribution of this document in unlimited

17. DISTRIBUTION STATEMENT *(of the abstract entered in Block 20, if different from Report)*

N/A

18. SUPPLEMENTARY NOTES

N/A

19. KEY WORDS *(Continue on reverse side if necessary and identify by block number)*

Key Words: CO_2 rebreathing, CSF, awake goats, CO_2 production

20. ABSTRACT *(Continue on reverse side if necessary and identify by block number)*

In awake goats before and after ablation of carotid bodies (CBx) we studied the effect of actue metabolic acidosis (AMA) produced by intravenous infusion of HCL on resting pulmonary ventilation, on composition of arterial blood and CSF, and on ventilatory responsiveness to hyperoxic CO_2 rebreathing. AMA caused decrease in $PaCO_2$ (breathing air at rest) and shifted position of CO_2 response curves toward lower values of PCO_2. These changes were similar before and after CBx, though the levels of PCO_2 in arterial blood during air breathing, and in

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

Unclassified

SECURITY CLASSIFICATION OF THIS PAGE *(When Data Entered)*

expired gas at a given level of ventilation during CO_2 rebreathing were higher after CBx. We conclude that a respiratory adaptation to AMA does occur in goats deprived of peripheral chemoreceptors, and is probably mediated by the central chemoreceptors.

DISPOSITION FORM

For use of this form, see AR 340-15; the proponent agency is The Adjutant General's Office.

REFERENCE OR OFFICE SYMBOL	SUBJECT
SGRD-UE-AR	Request for Clearance of Technical Paper (USARIEM)

THRU XXXXX Div
Medical Advisor

FROM Director
Altitude Rsch Div

DATE 26 May 1982 CMT 1

TO Commander, USARIEM

1. Reference USARIEM Memo 360-1, I request clearance of attached [X] manuscript, [ ] abstract, [ ] presentation, [ ] technical report, [ ] review article. Report Documentation Page, DD Form 1473 (is) (is not) attached.

Title Respiratory Adaptation to Acute Metabolic Acidosis in Goats with Ablated Carotid Bodies.

Author(s) R. A. Steinbrook, S. Javaheri, R. A. Gabel, J. C. Donovan, D. E. Leith and V. Fencl

Intended for publication in Journal of Applied Physiology: Respirat Environ Exercise Physiol.

Intended for presentation before _____

_____ Location _____ Date _____

2. Budget Project No. 3E161102BS10 Cost Code 24182101002

3. Attached contains no classified material. It meets accepted standards for scientific accuracy and propriety. It contains no potentially sensitive or controversial items.

JOHN T. MAHER, Ph.D.
Director
Altitude Research Division

Incl
as (6)

SGRD-UEZ ( )

THRU Chief, Admin Svc Br
XXXXX Div

FROM Commander

DATE 28 May 82 CMT 2

TO Dr. Maher

[ ] Clearance is granted.

[ ] Clearance is not granted.

[ ] This document must be forwarded to USAMRDC for clearance.

Please note a few typos.

ELIOT J. PEARLMAN
Colonel, MC
Commanding

NATICK FL 453
1 Mar 82 EDITION OF 1 SEP 80 IS OBSOLETE.

CLEARANCE NO. M34/82

DA FORM 1 FEB 82 2496 REPLACES DD FORM 96, EXISTING SUPPLIES OF WHICH WILL BE ISSUED AND USED UNTIL 1 FEB 83 UNLESS SOONER EXHAUSTED.

* U.S. GPO: 1974—540-843/8656

RESPIRATORY ADAPTATION TO ACUTE METABOLIC ACIDOSIS IN GOATS WITH ABLATED CAROTID BODIES.

R.A. Steinbrook, S. Javaheri*, R.A. Gabel,

J.C. Donovan, D.E. Leith, and V. Fencl

U.S. Army Research Institute of Environmental Medicine, Natick, 01760; and Departments of Anesthesia and Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts 02115.

Abbreviated title: Metabolic acidosis and chemodenervation

Correspondence to:

Vladimir Fencl, M.D.
Department of Medicine
Brigham and Women's Hospital
75 Francis Street
Boston, MA 02115

(617) 732-6738

ABSTRACT

In awake goats before and after ablation of carotid bodies (CBx) we studied the effect of acute metabolic acidosis (AMA) produced by intravenous infusion of HCl on resting pulmonary ventilation, on composition of arterial blood and CSF, and on ventilatory responsiveness to hyperoxic CO_2 rebreathing. AMA caused decrease in $PaCO_2$ (breathing air at rest) and shifted the position of CO_2 response curves toward lower values of PCO_2. These changes were similar before and after CBx, though the levels of PCO_2 in arterial blood during air breathing, and in expired gas at a given level of ventilation during CO_2 rebreathing were higher after CBx. We conclude that a respiratory adaptation to AMA does occur in goats deprived of peripheral chemoreceptors, and is probably mediated by the central chemoreceptors.

Key words: CO_2 rebreathing, CSF, awake goats, CO_2 production

INTRODUCTION

Acid-base disturbances of primarily metabolic origin elicit respiratory compensation. In metabolic acidosis, $PaCO_2$ is lowered, which alleviates the acidemia. An opposite change in $PaCO_2$ occurs in primary metabolic alkalosis. Furthermore, the ventilatory responses to increase in $PaCO_2$ produced by CO_2 inhalation are shifted to lower values of $PaCO_2$ in metabolic acidosis, and to higher $PaCO_2$ values in metabolic alkalosis. The roles played by the carotid bodies (CB) and by the central chemoreceptors in these respiratory adaptations are disputed. A predominant role was ascribed to central chemoreceptors by Pappenheimer (20) and Fencl et al (7), while Mitchell (17) and Bainton (1) concluded from their studies in awake dogs that excision of CB (CBx) abolishes the respiratory response to primary metabolic acid-base disturbances. More recently, Javaheri et al (12) and Kaehny et al (13) reported that in dogs, metabolic acidosis does stimulate ventilation in the absence of CB.

In awake goats before and after CBx, we studied the effect of acute metabolic acidosis (AMA), on resting pulmonary ventilation, on composition of arterial blood and CSF, and on responsiveness to CO_2 rebreathing. Respiratory adaptation to AMA did occur in goats deprived of function of CB. It was manifested by decrease in the resting $PaCO_2$ and by a shift of the CO_2 response curves to lower PCO_2 values.

METHODS

General

The studies were performed in four awake goats weighing 36-44 kg (mean 40 kg), surgically prepared with carotid loops and with implanted

occipital guide tubes for sampling of cisternal CSF. The same animals were used in another study (26). On each experimental day we punctured the cistern through the guide tube, percutaneously inserted a plastic cannula into the carotid artery in the loop and inserted another into the superior vena cava through the contalateral external jugular vein. Carotid arterial blood pressure was continuously monitored with a transducer (Statham 23DB). We measured resting ventilation ($\dot{V}_E$) and CO_2 production ($\dot{V}_{CO_2}$), and sampled arterial blood and cisternal CSF while the goats inhaled room air. Next we measured the ventilatory response to hyperoxic CO_2 rebreathing. We then induced AMA by infusing 0.2 N HCl in isotonic saline into the superior vena cava. The total dose of HCl was 3 mM/kg of body weight, delivered over approximately one hour at a steady rate, unless there was indication for slowing the rate. Occasional extrasystoles and bradycardia were observed in some animals during the first minutes of infusion. The goats appeared calm during the infusion. Fifteen to twenty minutes after completion of the infusion, we repeated measurements of $\dot{V}_E$ and $\dot{V}_{CO_2}$, sampling of arterial blood and cisternal CSF, and testing by CO_2 rebreathing. Each animal was studied twice before and twice four to five weeks after CBx. Means of the two measurements in each condition were used for data analysis. Completeness of CBx was tested by measuring the ventilatory response to acute hypoxia and to injection of cyanide (1 μM/kg BW) as described and reported previously (26).

Respiratory Measurements

The techniques have previously been described in detail (26).

In brief, the goats wore latex rubber masks and breathed through a low resistance non-rebreathing valve (J-valve, Model P-307, dead space 92 ml, Warren E. Collins). Volume of expired gas was measured with a Wedge spirometer (Med-Science Electronics). Concentrations of CO_2 and O_2 at the airway were measured with an infrared analyzer (Beckman LB-2) and a mass spectrometer (Perkin Elmer, MGA 1100A). All measured variables were recorded on a strip chart (Gould Brush Model 200), and on a magnetic tape (Hewlett Packard Model 3968). Ventilation was calculated breath-by-breath with a computer. Alveolar ventilation ($\dot{V}_A$) was calculated using Enghoff's modification of Bohr's formula for respiratory dead space. All ventilatory data were normalized to body weight 40 kg.

For hyperoxic CO_2 rebreathing, a modification (26) of Read's technique (23) was used. Linear regressions were derived for minute ventilation (on a breath-by-breath basis) as a function of the simultaneously measured end-tidal PCO_2 (P_{ETCO_2}). Ventilatory responsiveness to CO_2 was compared using slopes of these regressions and values of $\dot{V}_E$ at P_{ET} = 60 torr.

Analytical Techniques

Radiometer electrodes and electronics (BMS 2MK2) were used to measure PCO_2, PO_2 and pH in arterial blood and CSF at 37C, with correction to rectal temperature (10, 18). CO_2 concentrati- (C_{CO_2}) in CSF was measured with a Natelson microgasometer (Scientific Industries), and $[Cl^-]$ in anaerobically separated plasma and in CSF by potentiometric titration (Aminco-Cotlove, American Instruments). Bicarbonate in plasma and in CSF was calculated from measured pH and PCO_2 or

C_{CO_2}, applying published values for pK' and CO_2 solubilities (18). Base excess (BE) was determined with a Blood Gas Calculator (25).

Statistical Analyses

Student's t-test, analysis of variance, or a non-parametric test of variance (4) was applied, as indicated.

RESULTS

CBx abolished the ventilatory response to acute hypoxia (PaO_2 45-60 torr for 5-10 minutes) in these goats, as reported previously (26). When CB were intact, hypoxia increased $\dot{V}_E$ from its mean normoxic (PaO_2 85-95 torr) value of 11.7 ± 1.9 to 14.3 ± 1.6 l/min BTPS ($p < 0.05$). After CBx, $\dot{V}_E$ was not statistically different during normoxia and acute hypoxia (10.8 ± 1.1 and 11.3 ± 0.9 l/min BTPS, respectively).

The effects of CBx and AMA on resting pulmonary ventilation, and on the composition of arterial blood and CSF, are shown in Table 1. CBx produced a decrease in $\dot{V}_{CO_2}$ and hypoventialtion with a mild but statistically significant hypercapnia; in CSF, no significant changes occurred in the mean values of PCO_2 and pH. These findings are similar to those we have reported in a group of five awake goats (26). The standard infusion of HCl produced an AMA of similar severity before and after CBx. The mean (± S.E.) change in BE during AMA was -9.1 ± 0.8 and -7.7 ± 0.9 mE/l in intact and chemodenervated goats, respectively (not different by t-test for paired samples or by ranking test of variance). Mean values of BE, $[Cl^-]$ and $[HCO_3^-]$ in arterial

Table 1

blood plasma during AMA were similar before and after CBx (Table 1).

In spite of the resting hypercapnia observed after CBx during normal metabolic acid-base balance, $PaCO_2$ decreased in response to AMA after CBx, as it did before chemodenervation. When CB were intact, AMA caused reduction in mean $PaCO_2$ from 37.1 to 33.0 torr ($p < 0.05$); after CBx, mean $PaCO_2$ decreased with AMA from 39.7 to 35.7 torr ($p < 0.05$). Mean (± S.E.) change in $PaCO_2$ in response to AMA was -3.4 ± 0.7 and -4.0 ± 1.4 torr in intact and in chemodenervated goats, respectively. The mean (± S.E.) decrease in $PaCO_2$ per unit of acute base deficit ($\Delta PaCO_2/\Delta BE$) was 0.37 ± 0.07 $(mE/l)^{-1}$ before CBx, and 0.53 ± 0.17 torr $(mE/l)^{-1}$ after chemodenervation ($p < 0.05$, by ranking test of variance). Thus the hyperventilation elicited by AMA was not less after CBx, and it appeared even somewhat more pronounced with ablated CB, although this was not detected in our measurements of resting ventilation possibly owing to a small decrease in $\dot{V}_{CO_2}$ during AMA (Table 1).

In CSF, mean PCO_2 was the same before and after CBx when the goats were in normal metabolic acid-base balance (Table 1, [26]). AMA caused a decrease in CSF PCO_2 both before and after CBx, but the mean (± S.E.) change was smaller after CBx than before (-3.3 ± 0.7 and -5.0 ± 1.2 torr, respectively; $p < 0.05$, ranking test of variance). Thus, during AMA, mean CSF PCO_2 was higher after CBx than before (41.6 vs 38.8 torr). In both conditions, a small increase in mean $[Cl^-]$ was manifest during AMA, with reciprocal change in $[HCO_3^-]$ ($p < 0.05$). CSF pH did not change with AMA before or after CBx.

During normal acid-base balance, the mean (± S.E.) difference between PCO_2 in CSF and in arterial blood ($P_{csf_{CO2}} - PaCO_2$) was 7.0 ± 1.0 and

4.9 ± 0.3 torr ($p < 0.05$) before and after CBx, respectively (26). In response to AMA, this difference was reduced when CB were intact (Figure 1), on the average by -1.8 ± 0.8 torr. In contrast, with

Figure 1

CB ablated, ($P_{csf_{CO_2}}$ - $PaCO_2$) increased in response to AMA in 3 of 4 observations, on the average by +1.5 ± 0.9 torr. These changes in ($P_{csf_{CO_2}}$ - $PaCO_2$) during AMA in intact and chemodenervated goats are statistically different ($p < 0.05$ by t-test for paired samples; $p < 0.001$ by ranking test of variance).

Data on hyperoxic CO_2 rebreathing are summarized in Table 2 and Figure 2. In the normal metabolic acid-base balance, CBx produced a

Table 2

statistically significant ($p < 0.01$) shift of the CO_2 response curves to higher $P_{ET_{CO_2}}$ values, as indicated by a decrease in the value of $\dot{V}_E$ at $P_{ET_{CO_2}}$ = 60 torr. However, the slopes of the curves were not significantly different, as previously reported (26). AMA produced a change in the ventilatory response to CO_2 that was similar before

Figure 2

and after CBx. Slopes of the curves did not change significantly with AMA either before or after CBx, but in both conditions, AMA caused a statistically significant increase in the mean values of $\dot{V}_E$ at $P_{ET_{CO_2}}$ = 60 torr, indicating that position of the CO_2 response curves was shifted to lower $P_{ET_{CO_2}}$ values.

DISCUSSION

We have shown in a previous communication (26) that the goats used in the present study were deprived of peripheral chemoreception after CBx: the ventilatory response to hypoxia of 5-10 minutes duration was abolished, and during hyperoxia (PaO_2 > 300 torr for

5-10 minutes), pulmonary ventilation was increased; stimulation of ventilation by acute hyperoxia typically occurs in chemodenervated animals (5, 16).

Surprisingly, the resting $\dot{V}_{CO_2}$ was decreased after CBx, by almost 20 percent. Data of Forster et al (9) also show a statistically significant decrease in $\dot{V}_{CO_2}$ in chemodenervated goats. However, $\dot{V}_A$ decreased more than did $\dot{V}_{CO_2}$; therefore, $PaCO_2$ was elevated both in our observations and in those of Forster et al. Starting from these higher baseline $PaCO_2$ values, chemodenervated goats lowered their resting $PaCO_2$ in response to AMA, just as they did when the CB were intact. The degree of lowering of $PaCO_2$ in relation to base deficit in blood was even greater after CBx. Thus, a ventilatory response to AMA was manifest in the chemodenervated awake goats. This is in agreement with findings in anesthetized cats (14) and in anesthetized (12) and awake dogs (13); but these findings are at variance with those of Mitchell (17) and of Bainton (1) in awake dogs. We have no explanation for this discrepancy. In our results, CO_2 response curves were shifted to lower PCO_2 values by induction of AMA, both before and after CBx. Similar results were obtained in anesthetized cats by Katsaros (14). It appears that a respiratory adaptation to AMA, manifest in lowering the resting $PaCO_2$ and in shifting CO_2 response curves to lower PCO_2 values, does occur in goats with ablated CB.

The question arises whether the observed respiratory adaptation to AMA could be mediated by the central chemoreceptors, as postulated by Pappenheimer (20) and Fencl et al (7) for stable metabolic acidosis. The stimulus for the central chemoreceptors is believed to be increase

in $[H^+]$ in the cerebral interstitial fluid (cISF) that surrounds the receptors (7, 19). In stable metabolic acid-base disturbances of several days' duration, $[H^+]$ in cisternal CSF appears to approximate $[H^+]$ in cISF (7, 20). However, during acutely developing metabolic acidosis, a "paradoxical" alkaline shift in CSF pH can be seen in spontaneously breathing animals (24). This results from the high permeability of the blood-brain barrier for CO_2 on one hand, and the low permeability of the blood-CSF barrier for ions on the other. As ventilation is stimulated by the metabolic acidosis, PCO_2 in brain tissue and in cisternal CSF decreases before any change in CSF $[HCO_3^-]$ occurs.

We sampled CSF about 1 hour after termination of HCl infusion. PCO_2 in CSF was lowered at that time, both before and after CBx, however, we did not observe an alkaline shift in CSF pH. There was an indication that $[HCO_3^-]$ had begun to decrease, and $[Cl^-]$ to increase in CSF at the time of sampling. In such transient states, large-cavity CSF does not reflect the composition of cISF (6, 11, 15). In experiments in which pH was measured by electrodes attached to brain surface, and cerebral-tissue PCO_2 derived from measured PCO_2 values in arterial and sagittal sinus blood (22) it was found that in the fluid underlying the pH electrode (which presumably approximates cISF), $[H^+]$ increased and $[HCO_3^-]$ decreased within minutes after induction of acute metabolic acidosis, before any change in $[HCO_3^-]$ in cisternal CSF was detected (6, 11). It is thus possible that stimulation of central chemoreceptors by increased $[H^+]$ in cISF plays a role in respiratory adaptations to AMA (12) similar to that proposed for stable acid-base

disturbances (7, 20).

In chemodenervated goats, the values of PCO_2 in arterial blood while breathing air, and PET_{CO_2} values at a given $\dot{V}_E$ during CO_2 rebreathing, were higher than before CBx, both before and during AMA. However, the changes in these PCO_2 values produced by AMA were similar before and after CBx. Perhaps in the regulation of these adaptations to AMA, the input from CB influences the set-point, while gain of the controller reflects input from the central chemoreceptors.

PCO_2 in cisternal CSF approximates the cerebral-tissue PCO_2 (22). The difference between cisternal CSF PCO_2 and $PaCO_2$ (ΔPCO_2) is mainly a function of cerebral blood flow (in relation to cerebral CO_2 production). While CB were intact, this ΔPCO_2 was reduced during AMA, suggesting a (relative) increase in cerebral blood flow. This was similar to findings in awake dogs (3) and in humans (8) in metabolic acidosis. However, after CBx, the mean ΔPCO_2 increased with AMA. This may suggest that the regulation of cerebral blood flow in response to AMA was changed after CBx. Cerebral vasodilation in response to hypercapnia and hypoxia was found to be reduced in anesthetized animals after CBx (21); this was not confirmed in another study (2). It has been shown that cerebral vascular responses to stimulation of peripheral chemoreceptors and baroreceptors can be altered by general anesthesia (27). Measurements of cerebral blood flow in intact awake animals are needed to determine whether CB have any role in the regulation of cerebral blood flow (and of cerebral-tissue PCO_2) in response to acid-base disturbances.

Footnote (on front page)

* Present address: Laboratorium voor Normale en Pathologische Fysiologie, Rijksuniversiteit, Ghent, Belgium.

Acknowledgements

We thank Ella Munro and Henry Feldman, Ph.D., for help with statistical analyses. The excellent technical support of Genevieve Farese, Linda Farley, Vincent Forte, and Louise Price is gratefully acknowledged.

This study was supported in part by NIH Pulmonary SCOR Grant HL 19170.

The views, opinions, and/or findings in this report are those of the authors and should not be construed as an official Department of Army position, policy, or decision, unless so designated by other official documentation.

Presented in part at the 65th Annual Meeting of the Federation of American Societies for Experimental Biology, 12-17 April 1981, Atlanta, GA.

References

1. Bainton, C.R. Canine ventilation after acid-base infusions, exercise, and carotid body denervation. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 44: 28-35, 1978.

2. Bates, D., and T.M. Sundt, Jr. The relevance of peripheral baroreceptors and chemoreceptors to regulation of cerebral blood flow in the cat. Circulation Res. 38: 488-493, 1976.

3. Chazan, J.A., F.M. Appleton, A.M. London, and W.B. Schwartz. Effects of chronic metabolic acid-base disturbances on the composition of cerebrospinal fluid in the dog. Clin. Sci. 36: 345-358, 1969.

4. Conover, W.J. Practical Nonparametric Statistics. New York: J. Wiley & Sons, 1971.

5. Davenport, H.W., G. Brewer, A.F. Chambers, and S. Goldschmidt. The respiratory responses to anoxemia of unanesthetized dogs with chronically denervated aortic and carotid chemoreceptors and their causes. Am. J. Physiol. 148: 406-416, 1947.

6. Fencl, V., J.R. Dmochowski, and A.E. Young. Dynamics of ionic composition of cerebral interstitial fluid in acute metabolic acid-base disturbances. Proc. Internat. Union Physiol. Sci. 13: 223, 1977.

7. Fencl, V., T.B. Miller, and J.R. Pappenheimer. Studies on the respiratory response to disturbances of acid-base balance, with deductions concerning the ionic composition of cerebral interstitial fluid. Am. J. Physiol. 210: 459-472, 1966.

8. Fencl, V., J.R. Vale, and J.A. Broch. Respiration and cerebral blood flow in metabolic acidosis and alkalosis in humans. J. Appl. Physiol. 27: 67-76, 1969.

9. Forster, H.V., G.E. Bisgard, and J.P. Klein. Effect of peripheral chemoreceptor denervation on acclimatization of goats during hypoxia. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 50: 392-398, 1981.

10. Gabel, R.A. Algorithms for calculating and correcting blood-gas and acid-base variables. Respir. Physiol. 42: 211-232, 1980.

11. Javaheri, S., A. Clendening, N. Papadakis, and J.S. Brody. Change in brain surface pH during acute isocapnic metabolic acidosis. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 51: 276-281, 1981.

12. Javaheri, S., L. Herrera, and H. Kazemi. Ventilatory drive in acute metabolic acidosis. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 45: 913-918, 1979.

13. Kaehny, W.D., and J.T. Jackson. Respiratory response to HCl acidosis in dogs after carotid body denervation. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 46: 1138-1142, 1979.

14. Katsaros, B. Die Rolle der Chemoreceptoren des Carotisgebiets der narkotisierten Katze für die Antwort der Atmung auf isolierte Änderung der Wasserstoffionen-Konzentration und des CO_2-Drucks des Blutes. Pflügers Arch. 282: 157-178, 1965.

15. Loeschcke, H.H. and H.R. Ahmad. Transients and steady-state chloride-bicarbonate relationship of brain extra-cellular fluid. In: Biophysics and Physiology of Carbon Dioxide,

edited by C. Bauer, G. Gros, and H. Bartels. New York: Springer, 1980, p. 439-448.

16. Miller, M.J., and S.M. Tenney. Hyperoxic hyperventilation in carotid-deafferented cats. Respir. Physiol. 23: 23-30, 1975.

17. Mitchell, R.A. The regulation of respiration in metabolic acidosis and alkalosis. In: Cerebrospinal Fluid and the Regulation of Ventilation, edited by C. McC. Brooks, F.F. Kao, and B.B. Lloyd. Oxford: Blackwell, 1965, p. 109-131.

18. Mitchell, R.A., D.A. Herbert, and C.T. Carman. Acid-base constants and temperature coefficients for cerebrospinal fluid. J. Appl. Physiol. 20: 27-30, 1965.

19. Mitchell, R.A., H.H. Loeschcke, W.H. Massion, and J.W. Severinghaus. Respiratory responses mediated through superficial chemosensitive areas of the medulla. J. Appl. Physiol. 18: 523-533, 1963.

20. Pappenheimer, J.R. The ionic composition of cerebral extracellular fluid and its relation to control of breathing. Harvey Lect. 6: 71-93, 1967.

21. Ponte, J., and M.J. Purves. The role of the carotid body chemoreceptors and carotid sinus baroreceptors in the control of cerebral blood vessels. J. Physiol., London. 237: 315-340, 1974.

22. Pontén, U., and B.K. Siesjö. Gradients of CO_2 tension in the brain. Acta Physiol. Scand. 67: 129-140, 1966.

23. Read, D.J.C. A clinical method for assessing the ventilatory response to carbon dioxide. Australas. Ann. Med. 16: 20-32, 1967.

24. Robin, E.D., R.D. Whaley, C.H. Crump, A.G. Bickelmann, and D.M. Travis. Acid-base relations between spinal fluid and arterial blood with special reference to control of ventilation. J. Appl. Physiol. 13: 385-392, 1958.

25. Severinghaus, J.W. Blood gas calculator. J. Appl. Physiol. 21: 1108-1116, 1966.

26. Steinbrook, R.A., J.C. Donovan, R.A. Gabel, D.E. Leith, and V. Fencl. Ventilatory responsiveness of goats with ablated carotid bodies. J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. (submitted).

27. Vatner, S.F., L.L. Priano, J.D. Rutherford, and W.T. Manders. Sympathetic regulation of the cerebral circulation by the carotid chemoreceptor reflex. Am. J. Physiol. 238: H594-H598, 1980.

TABLE 1

Effects of ablation of the carotid bodies and of acute metabolic acidosis on pulmonary ventilation and on composition of arterial blood and CSF.

				Arterial Blood						CSF			
	$\dot{V}_E$ l/min BTPS	$\dot{V}_A$ l/min BTPS	$\dot{V}_{CO_2}$ ml/min STPD	pH	PCO_2 torr	PO_2 torr	BE mE/l	$[HCO_3^-]$ mM/l	$[Cl^-]$ mM/l	pH	PCO_2 torr	$[HCO_3^-]$ mM/l	$[Cl^-]$ mM/l
CB intact													
Control	10.5±0.5	4.6±0.2	204± 6	7.423±0.005	37.1±1.0	93±1	-0.3±0.5	23.7±0.5	112±2	7.306±0.013	44.4±1.2	23.7±0.4	132±1
AMA	11.3±1.2	5.1±0.4	195±14	7.284±0.023	33.0±0.9	95±3	-10.1±1.4	15.4±1.2	123±2	7.308±0.004	38.8±1.0	22.8±0.3	134±3
CB ablated													
Control	8.0±0.4	3.7±0.3	165± 7	7.399±0.004	39.7±0.8	86±2	-0.7±0.7	23.6±0.6	112±1	7.307±0.011	44.6±0.6	24.8±0.5	130±1
AMA	7.8±0.3	3.8±0.2	157± 6	7.286±0.013	35.7±1.3	91±2	-9.0±0.9	16.2±0.8	120±2	7.306±0.015	41.6±0.6	23.6±0.2	131±1
Analysis of variance:													
Effect of CBx on variables during control periods:													
p	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	NS	NS	NS	NS	NS	NS	NS
Effect of CBx on variables during AMA:													
p	<0.05	<0.05	NS	NS	NS	NS	NS	NS	NS	NS	<0.05	NS	NS
AMA vs Control, CB intact:													
p	NS	NS	NS	<0.005	<0.05	NS	<0.005	<0.001	<0.01	NS	<0.05	<0.05	NS
AMA vs control, CBx:													
p	NS	NS	NS	<0.005	<0.05	<0.05	<0.005	<0.001	<0.01	NS	<0.05	<0.05	NS

Values are means ± S.E. of repeated measurements in 4 goats. CB: carotid bodies; CBx: ablated CB; Control: normal metabolic acid-base balance; AMA: acute metabolic acidosis.

TABLE 2

Ventilatory response to hyperoxic CO_2 rebreathing of awake goats.

	$\dot{V}_E$ at P_{ETCO_2} = 60 torr l/min, BTPS	Slope of CO_2 response curves l/(min x torr)
Carotid bodies intact		
Control	29.5 ± 6.7	3.5 ± 0.4
AMA	43.0 ± 7.3*	3.6 ± 0.1
Carotid bodies ablated		
Control	17.3 ± 2.6†	2.9 ± 0.3
AMA	23.8 ± 3.6*†	3.2 ± 0.3

Analysis of variance:

* AMA significantly different from control ($p < 0.05$).

† Significantly different from the value with carotid bodies intact ($p < 0.05$).

Values are means ± S.E. of repeated measurements in 4 goats ($Pa_{O_2} > 300$ torr).

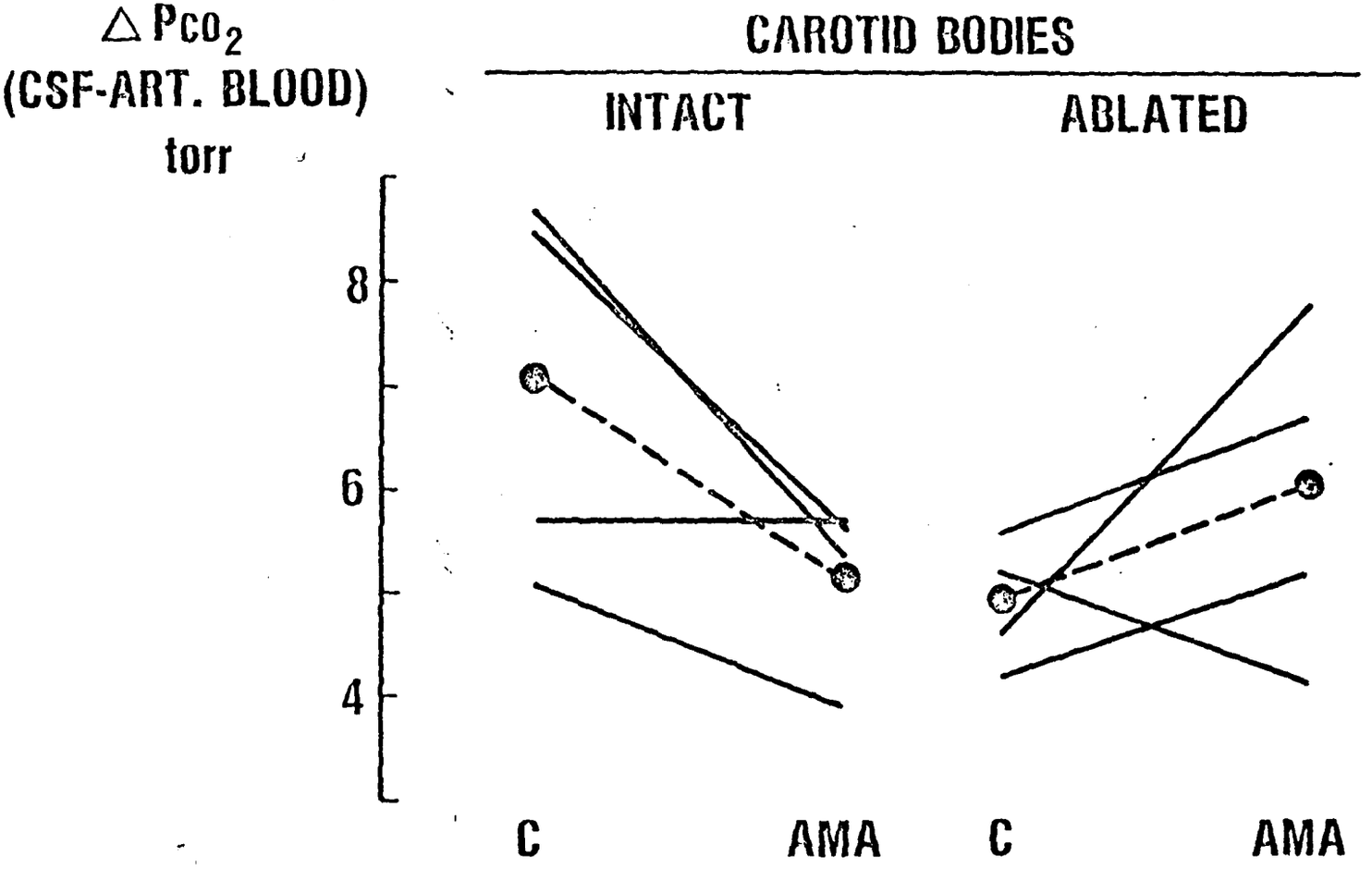
Control: normal metabolic acid-base balance; AMA: acute metabolic acidosis (base deficit -9 to -10 mE/l).

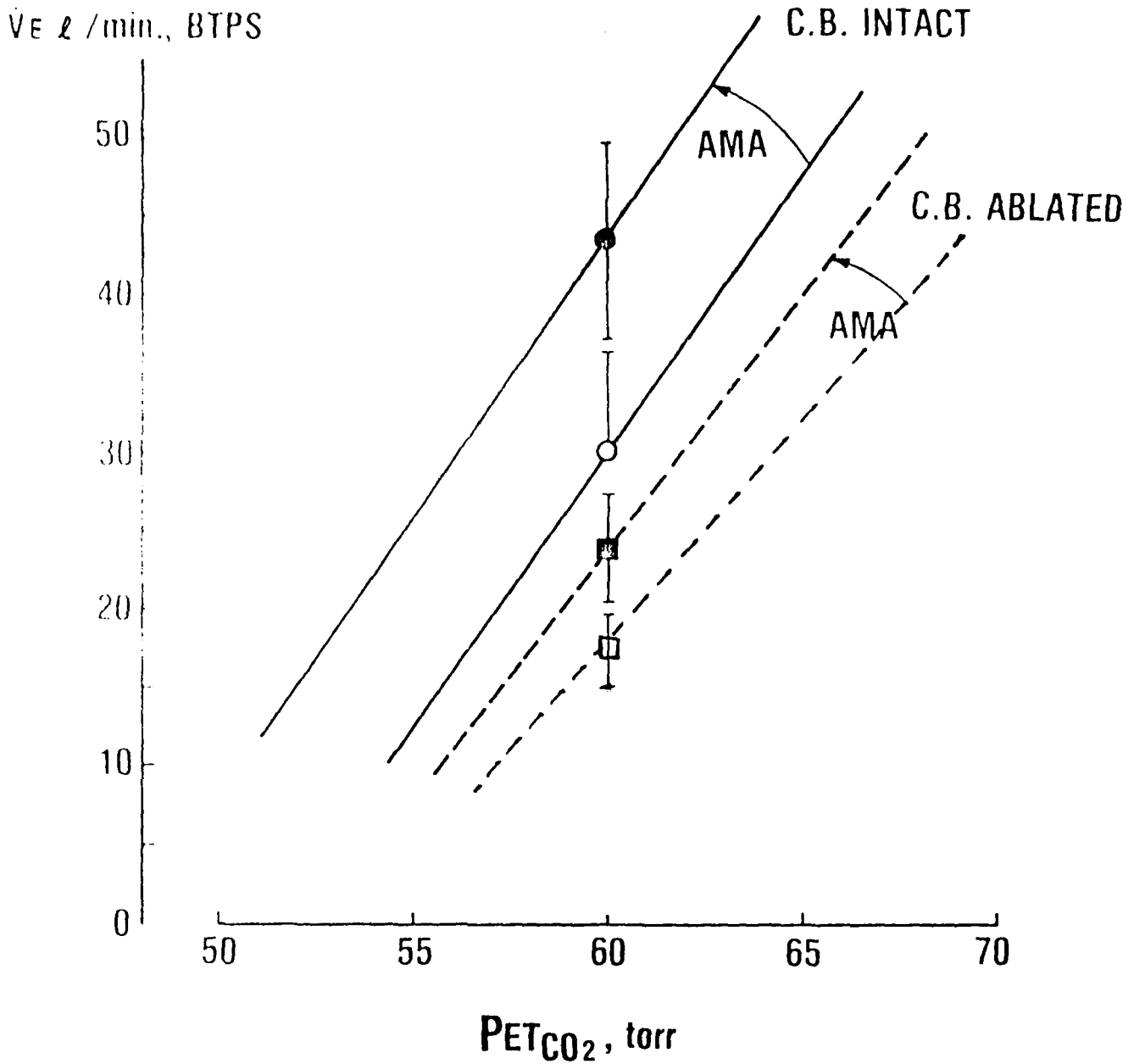
LEGENDS TO FIGURES

Figure 1. Effect of acute metabolic acidosis (AMA) on the difference in PCO_2 between cisternal CSF and arterial blood in goats with intact and ablated carotid bodies. The points joined by a broken line indicate mean values. C: Control (normal metabolic acid-base balance).

Figure 2. Effect of ablation of carotid bodies and of acute metabolic acidosis (AMA) on ventilatory responses to hyperoxia (PaO_2 > 300 torr) CO_2 rebreathing. Constructed from mean values of $\dot{V}_E$ at P_{ETCO_2} = 60 torr, and from mean values of slopes of the plots $\dot{V}_E$ vs P_{ETCO_2}. See Table 2 for numerical data. Open symbols: mean (± S.E.) values of $\dot{V}_E$ at P_{ETCO_2} = 60 torr in normal metabolic acid-base balance. Closed symbols apply to AMA.

Fig 1


Δ Pco2
(CSF-ART. BLOOD)
torr
CAROTID BODIES
INTACT
ABLATED
8
6
4
C
AMA
C
AMA


VE ℓ /min., BTPS
C.B. INTACT
AMA
C.B. ABLATED
AMA
50
40
30
20
10
0
50
55
60
65
70
PETCO2, torr

The views, opinions, and/or findings contained in this report are those of the author(s) and should not be construed as an official department of the Army position, policy, or decision, unless so designated by other official documentation.